

## PATENT SPECIFICATION

NO DRAWINGS

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## COMPLETE SPECIFICATION

## Preparations for the Treatment of Udders of Dairy Animals

We, FARBWERKE HOECHST AKTIENGESELLSCHAFT, Vormals Meister Lucius & Brüning, a Company recognized by German law, of 6230 Frankfurt (M)-Hoeschst, Germany, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

It is known to add dyestuffs to antibiotic-containing preparations for the treatment of mastitis, the dyestuff serving to indicate contamination of the milk with the antibiotic. The dyestuffs hitherto proposed for this purpose have the disadvantage that they are not excreted concurrently with the antibiotics. As a consequence, this may have the effect that under unfavourable circumstances the milk is not coloured although it contains antibiotics or that it is coloured but no longer contains antibiotic. Furthermore, in the case of penicillin concentrations of about 0.1 I.U./ml, these dyestuffs are unsatisfactory since they do not permit a determination of the colour of the milk with the naked eye. For the determination of concentrations of antibiotics which are smaller than the afore-said concentration, ion exchange methods or microbiological tests are usually applied; these methods, however, are too complicated for general use.

It is an object of the present invention to provide a coloured antibiotic-containing preparation for the treatment of the udders of dairy animals which not only cures the disease, but also indicates the excretion of the antibiotic with the milk by colouring the milk according to the degree of contamination with the antibiotic.

The present invention provides a penicillin-containing preparation for the treatment of udders of dairy animals which also contains, as an indicator of the penicillin excreted with the milk, the dyestuff Lebensmittelblau No. 3 advantageously in a quantity of 100 to 750

mg, preferably 250 to 500 mg, per dosage unit (or one teat), the proportion of penicillin to dyestuff being in the range of from 0.5 to 1 to 2 to 1, preferably from 0.8 to 1 to 1.2 to 1 by weight.

After the treatment of the udders with the preparation of the invention, the penicillin is excreted by the udders concurrently with the dyestuff so that penicillin concentrations of down to 0.03 I.U./ml of milk can be determined with the naked eye by the colour of the milk. A milk which contains penicillin in a concentration of 0.03 I.U./ml is generally considered harmless; it can be further treated and consumed.

The dyestuff used according to the invention is an officially allowed food dyestuff and is free from harmful substances. It does not affect the tissue of the udders and also does not reduce the antibiotic activity of the antibiotics used.

The dyestuff Lebensmittelblau No. 3 used according to the invention is also known under the name Patentblau No. 5 and under the chemical designation 2,4-disulpho-5-hydroxy-4',4'' - bis - (diethylamino) - triphenyl - carbinol (calcium salt). Furthermore, it is defined under Colour Index No. 42051, Schultz No. 826 and E.E.C. No. E 131.

The preparations which may be coloured with Lebensmittelblau No. 3 with the afore-said effect include penicillin-containing, aqueous or oily suspensions. Under the term penicillin are to be understood all types of penicillin and the salts thereof with any base. For example, there may be mentioned procaine-penicillin which has proved to be a highly effective antibiotic in the treatment of mastitis. In addition to penicillin, the preparations may also contain other antibiotics, for example, streptomycin, neomycin, dihydrostreptomycin, bacitracin and other antibacterially active substances, for example, sulphonamides or nitrofurans derivatives, as well as

the additives usual in pharmaceutical preparations, for example, solubilizer, adjuvants or stabilizers. Aqueous suspensions may also be combined with buffer substances for the regulation of the pH-values. For oily suspensions, there may be used as the base all pharmaceutically suitable oils, for example glycerides such as castor oil or sesame oil or also mineral oils such as paraffin oil and correspondingly composed synthetic oils for example, synthetic glycerides, as well as mixtures of the aforesaid oils.

The treatment of the udders with the coloured preparations of the present invention does not require special measures. The preparation can be introduced by means of a suitable syringe through the teat canal into the milk cistern and milk ducts of the udder.

The animals which may be treated with the preparations of the invention include all dairy animals, for example cows, ewes or goats, the milk of which is used for alimentary purposes.

After the treatment with the composition of the present invention, the milk of the animals treated shows a significant blue colour which is recognizable with the naked eye all the time the penicillin content of the milk is not below the critical value of 0.03 I.U./ml. In addition, it is possible to determine quantitatively the degree of penicillin contamination of the milk by comparing the intensity of the colour with that of a comparison scale.

The excretion of penicillin and of dyestuff into the milk may last from one to several days, depending on the type of carrier substance and on the concentration of active substance. By reason of the concurrency of the excretion of penicillin and dyestuff in the system described, the milk obtained contains in any case as long as it is coloured penicillin in a concentration above the tolerance limit and if it is not coloured it does not contain the active substance in a harmful quantity.

The following Examples illustrate some preparations in accordance with the invention:—

## EXAMPLE 1:

Procaine-penicillin	46.00 mg.
Trisodium citrate	15.00 mg.
Lebensmittelblau No. 3	50.00 mg.
Distilled water	ad 1.00 ml.

## EXAMPLE 2:

Procaine-penicillin	46.00 mg.
Dihydrostreptomycin sulphate	29.00 mg.
Trisodium citrate	15.00 mg.
Lebensmittelblau No. 3	50.00 mg.
Distilled water	ad 1.00 ml.

## EXAMPLE 3:

Procaine-penicillin	46.00 mg.	60
Lebensmittelblau No. 3	50.00 mg.	
Sesame oil	ad 1.00 ml.	

## EXAMPLE 4:

Procaine-penicillin	46.00 mg.	
Dihydrostreptomycin sulphate	29.00 mg.	65
Lebensmittelblau No. 3	50.00 mg.	
Sesame oil	ad 1.00 ml.	

The normal dosages applied in therapy are generally higher than the amounts given in Examples 1 to 4. The Examples merely indicate some basic compositions given on the basis of 1 ml of final product.

## WHAT WE CLAIM IS:—

1. A penicillin-containing preparation for the treatment of udders of dairy animals, which contains as an indicator of the penicillin excreted with the milk, the dyestuff Lebensmittelblau No. 3 (as hereinbefore defined), the proportion of penicillin to dyestuff being in the range of from 0.5 to 1 to 2 to 1 by weight.

2. A preparation as claimed in claim 1, wherein the indicator dyestuff is present in a quantity of 100 to 750 mg. per dosage unit (for one teat).

3. A preparation as claimed in claim 1 or claim 2, wherein the indicator dyestuff is present in a quantity of 250 to 500 mg. per dosage unit (for one teat).

4. A preparation as claimed in any one of claims 1 to 3, wherein the proportion of penicillin to dyestuff is in the range of from 0.8 to 1 to 1.2 to 1 by weight.

5. A preparation as claimed in any one of claims 1 to 4, which also contains one or more other antibiotics.

6. A preparation as claimed in any one of claims 1 to 4, which also includes one or more substances selected from the group consisting of streptomycin, dihydrostreptomycin, neomycin, bacitracin, sulphonamides and nitro-furan derivatives.

7. A preparation as claimed in any one of claims 1 to 6, which also contains a pharmaceutically suitable carrier.

8. A preparation as claimed in claim 1 and as described in any one of the Examples herein.

9. A method for treating udder diseases of dairy animals with penicillin-containing preparations which comprises treating the udders of the said animals by intramammary injection with a preparation which contains in addition to penicillin the dyestuff Leben-

smittelblau No. 3 (as hereinbefore defined) as  
the indicator of the excreted penicillin.

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